

# PATENT COOPERATION TREATY

*IFD*

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

WOLF, GREENFIELD & SACKS, P.C.  
Attn. Oyer, Timothy J.  
Federal Reserve Plaza  
600 Atlantic Avenue  
Boston, MA 02210-2206  
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

|   |   |
|---|---|
| <p>Date of mailing<br/>(day/month/year) <span style="float: right;">06/05/2009</span></p> |   |
| <p>Applicant's or agent's file reference<br/>C1256.70001</p>                              | <p><b>FOR FURTHER ACTION</b>      See paragraphs 1 and 4 below</p>                                  |
| <p>International application No.<br/>PCT/US2008/010022</p>                                | <p>International filing date<br/>(day/month/year) <span style="float: right;">22/08/2008</span></p> |
| <p>Applicant<br/><br/>CLAROS DIAGNOSTICS, INC.</p>  |   |

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

**4. Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, within **20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

**RECEIVED**

Wolf, Greenfield & Sacks, P.C.

|   |   |
|---|---|
| <p>Name and mailing address of the International Searching Authority</p> <p> European Patent Office, P.B. 5818 Patentlaan 2<br/>NL-2280 HV Rijswijk<br/>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br/>Fax: (+31-70) 340-3016</p> | <p>Authorized officer</p> <p style="text-align: center;">Shara Atashi      <b>MAY 11 2009</b></p> <p style="text-align: right;">Docketed <input checked="" type="checkbox"/> Already Docketed <input type="checkbox"/><br/>Not Required <input type="checkbox"/> (See notes on accompanying sheet)<br/>Initials 1st <u>  </u> 2nd <u>  </u></p> |
|---|---|

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty; the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

**The amendments must be made in the language in which the international application is to be published.**

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### **"Statement under article 19(1)" (Rule 46.4)**

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### **Consequence if a demand for international preliminary examination has already been filed**

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

If a demand for international preliminary examination is made, the written opinion of the International Searching Authority will, except in certain cases where the International Preliminary Examining Authority did not act as International Searching Authority and where it has notified the International Bureau under Rule 66.1bis(b), be considered to be a written opinion of the International Preliminary Examining Authority. If a demand is made, the applicant may submit to the International Preliminary Examining Authority a reply to the written opinion together, where appropriate, with amendments before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later (Rule 43bis.1(c)).

### **Consequence with regard to translation of the international application for entry into the national phase**

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the *PCT Applicant's Guide*, Volume II.



# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |  |  |
|---|--|--|
| Applicant's or agent's file reference<br><b>C1256.70001</b> | <b>FOR FURTHER ACTION</b><br><small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small> |  |
| International application No.<br><b>PCT/US2008/010022</b>   | International filing date (day/month/year)<br><b>22/08/2008</b>  | (Earliest) Priority Date (day/month/year)<br><b>19/09/2007</b> |
| Applicant<br><br><b>CLAROS DIAGNOSTICS, INC.</b>            |  |  |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☐ the text is approved as submitted by the applicant  
☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 18  
☒ as suggested by the applicant  
☐ as selected by this Authority, because the applicant failed to suggest a figure  
☐ as selected by this Authority, because this figure better characterizes the invention  
b. ☐ none of the figures is to be published with the abstract

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2008/010022

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

Microfluidic systems including liquid containment regions (1206) and methods associated therewith for performing chemical, biological, or biochemical analyses are provided. Liquid containment regions (1206) of a microfluidic device may include regions that capture one or more liquids flowing in the device, while allowing gases or other fluids in the device to pass through the region. This may be achieved, in some embodiments, by positioning one or more absorbent materials (1208) in the liquid containment region (1206) for absorbing the liquids. This configuration may be useful for removing air bubbles from a stream of fluid and/or for separating hydrophobic liquids from hydrophilic liquids. In certain embodiments, the liquid containment region (1206) prevents any liquid from passing through the region. In some such cases, the liquid containment region may act as a waste area by capturing substantially all of the liquid in the device, thereby preventing any liquid from exiting the device. This arrangement may be useful when the device is used as a diagnostic tool, as the liquid containment region may prevent a user from being exposed to potentially-harmful fluids in the device.

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2008/010022

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
B01L G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No.         |
|-----------|--|-------------------------------|
| X<br>Y    | EP 0 430 248 A (MOCHIDA PHARM CO LTD [JP])<br>5 June 1991 (1991-06-05)<br>abstract; figures 5,6B,7B,8B,9B; example 6<br>page 5, lines 22-25<br>page 5, line 56 - page 6, line 2<br>page 6, lines 13-16 - lines 27-31<br>page 7, line 13 - page 8, line 44<br>page 10, lines 11-26 - page 13, lines 25-43 | 19-27,<br>29-38,40<br>1-18,28 |
| X         | EP 0 281 201 A (PB DIAGNOSTIC SYSTEMS INC [US]) 7 September 1988 (1988-09-07)<br><br>column 4, lines 25-58 - column 6, lines 1-41; figures 1,2,4-6<br>column 7, line 24 - column 8, line 8<br>column 8, line 31 - column 9, line 28<br><br>-----<br>-/--   | 19-27,<br>29,30,<br>32-40     |

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

3 February 2009

Date of mailing of the international search report

06/05/2009

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040,  
Fax: (+31-70) 340-3016

Authorized officer

Pessenda García, P

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/010022

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| Y         | WO 2005/072858 A (HARVARD COLLEGE [US];<br>SIA SAMUEL K [US]; LINDER VINCENT [CH];<br>WHITESID) 11 August 2005 (2005-08-11)<br>abstract; figures 13-15; examples 1-3<br>page 3, line 21 - page 4, line 19<br>page 8, lines 26-30 - page 13, lines 18-25<br>page 18, line 18 - page 19, line 15<br>page 20, line 29 - page 21, line 27<br>page 25, lines 16-22 - page 27, lines<br>25-29<br>page 28, lines 18-21<br>----- | 1-18, 28              |
| A         | US 2003/185713 A1 (LEONARD LESLIE [US] ET<br>AL) 2 October 2003 (2003-10-02)<br>paragraphs [0009], [0011], [0028] -<br>[0030], [0034], [0035]; figures<br>1, 2A-2C, 4A, 4B, 5B, 7<br>-----   | 1-40                  |
| A         | US 6 019 944 A (BUECHLER KENNETH F [US])<br>1 February 2000 (2000-02-01)<br>column 4, line 40 - column 5, line 8;<br>figures 1-1C<br>column 16, lines 60-66<br>-----   | 1-40                  |

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2008/010022

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-40

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-40

A method and a device including a microfluidic network for establishing flow of a first liquid in a channel, contacting at least a portion of the liquid with a reaction area; absorbing at least a portion of the liquid with an absorbent material contained in a liquid containment region positioned downstream of the reaction area, and controlling a rate of flow of a liquid in the channel, wherein the act of absorbing does not substantially modulate the flow rate of a liquid flowing in the channel upstream of the liquid containment region.

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2. claim: 41

A device including a microfluidic network, comprising: a first channel; a reaction area in fluid communication with the first channel; and an absorbent material and a disinfectant stored in a liquid containment region prior to use of the device, the liquid containment region positioned downstream of the reaction area and in fluid communication with the reaction area during use of the device.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/010022

| Patent document<br>cited in search report |    | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|---|----|---------------------|----------------------------|---------------------|
| EP 0430248                                | A  | 05-06-1991          | AU 642444 B2               | 21-10-1993          |
|   |    |                     | AU 6702690 A               | 06-06-1991          |
|   |    |                     | CA 2031001 A1              | 31-05-1991          |
|   |    |                     | US 5147607 A               | 15-09-1992          |
| EP 0281201                                | A  | 07-09-1988          | AU 605257 B2               | 10-01-1991          |
|   |    |                     | AU 1294988 A               | 26-09-1988          |
|   |    |                     | CA 1300006 C               | 05-05-1992          |
|   |    |                     | DE 3880531 D1              | 03-06-1993          |
|   |    |                     | DE 3880531 T2              | 09-09-1993          |
|   |    |                     | ES 2041775 T3              | 01-12-1993          |
|   |    |                     | FI 883599 A                | 04-09-1988          |
|   |    |                     | GR 3008296 T3              | 30-09-1993          |
|   |    |                     | JP 6016047 B               | 02-03-1994          |
|   |    |                     | JP 1502526 T               | 31-08-1989          |
|   |    |                     | NO 884658 A                | 19-10-1988          |
|   |    |                     | NZ 223637 A                | 28-05-1990          |
|   |    |                     | US 4918025 A               | 17-04-1990          |
|   |    |                     | WO 8806731 A1              | 07-09-1988          |
|   |    |                     | ZA 8800550 A               | 30-08-1988          |
| WO 2005072858                             | A  | 11-08-2005          | AU 2005209321 A1           | 11-08-2005          |
|   |    |                     | CA 2564211 A1              | 11-08-2005          |
|   |    |                     | EP 1776181 A1              | 25-04-2007          |
|   |    |                     | JP 2007524851 T            | 30-08-2007          |
| US 2003185713                             | A1 | 02-10-2003          | NONE                       |                     |
| US 6019944                                | A  | 01-02-2000          | US 5885527 A               | 23-03-1999          |

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

see form PCT/ISA/220

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2008/010022

International filing date (day/month/year)  
22.08.2008

Priority date (day/month/year)  
19.09.2007

International Patent Classification (IPC) or both national classification and IPC  
INV. B01L3/00

Applicant  
CLAROS DIAGNOSTICS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
Fax: +31 70 340 - 3016

Date of completion of  
this opinion

see form  
PCT/ISA/210

Authorized Officer

Pessenda García, P

Telephone No. +31 70 340-9874



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2008/010022

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2008/010022

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**Box No. IV Lack of unity of invention**

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1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☒ complied with
  - ☐ not complied with for the following reasons:
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-40

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

|                               |             |                    |
|-------------------------------|-------------|--------------------|
| Novelty (N)                   | Yes: Claims | <u>1-18,22,28</u>  |
|                               | No: Claims  | <u>19-27,29-40</u> |
| Inventive step (IS)           | Yes: Claims |                    |
|                               | No: Claims  | <u>1-40</u>        |
| Industrial applicability (IA) | Yes: Claims | <u>1-40</u>        |
|                               | No: Claims  |                    |

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

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International application No.  
PCT/US2008/010022

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**Box No. VIII    Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Re Item IV**

**Lack of unity of invention**

1. There are 4 independent claims:

Claim 1: A method comprising: establishing flow of a first plug comprising a first liquid and a second plug comprising a second liquid in a channel of a device including a microfluidic network, wherein the first and second plugs are separated by a fluid immiscible with the first and second liquids;  
contacting at least a portion of the first liquid and/or the second liquid with a reaction area of the network;  
absorbing at least a portion of the first liquid and/or the second liquid with an absorbent material contained in a liquid containment region positioned downstream of the reaction area, the containment region in fluid communication with the channel; and  
controlling a rate of flow of a liquid in the channel, wherein the act of absorbing does not substantially modulate the flow rate of a liquid flowing in the channel upstream of the liquid containment region.

Claim 19: A method, comprising: establishing flow of a first liquid in a channel of a device comprising a microfluidic network;  
causing a chemical and/or biological reaction to occur between a first component contained in the first liquid and a second component immobilized at a reaction area in fluid communication with the channel;  
passing a wash solution across the reaction area;  
absorbing at least a portion of the first liquid with an absorbent material contained in a liquid containment region in fluid communication with the channel; and  
controlling a rate of flow of a liquid in the channel,  
wherein the act of absorbing does not substantially modulate the flow rate of a liquid flowing in the channel upstream of the liquid containment region.

Claim 20: A device including a microfluidic network, comprising:  
a reservoir associated with the device, the reservoir containing a first liquid reagent stored therein prior to use of the device, in fluid communication with a first channel;  
a reaction area in fluid communication with the first channel during use of the device;

an absorbent material contained in a liquid containment region positioned downstream of the reaction area and in fluid communication with the reaction area during use of the device;  
an outlet positioned downstream of the liquid containment region; and  
a connecting channel fluidly connecting the outlet with the liquid containment region

Claim 41: A device including a microfluidic network, comprising:  
a first channel;  
a reaction area in fluid communication with the first channel; and  
an absorbent material and a disinfectant stored in a liquid containment region prior to use of the device, the liquid containment region positioned downstream of the reaction area and in fluid communication with the reaction area during use of the device.

It appears that within these independent claims unity does not exist for the following reasons:

A) The "same" or "corresponding" technical feature between these independent claims is that they relate to a device including a microfluidic network comprising a channel, a reaction area, and a liquid containment region having an absorbent material.

These features are already known from document **D1**(EP0430248) where a microfluidic device (Fig.5,[0030]) comprises a channel (51), a reagent-immobilized area (30) as a reaction area, and a fluid sump (90) having a absorbent material-accommodating area (80) with a water absorbent material (81).

Therefore, these features are not special (new and inventive) technical features. Thus, no "same" or "corresponding" special technical features could be found between the independent claims 1,19,20 and 41 as required by Rule 13.2 PCT.

B) Also the common problem underlying the invention, to retain one or more liquids within the device, preventing the liquids from exiting the device, is already known, see D1 (p.8 lines 7-11).



No other common problem could be found which could serve as the general inventive concept required by Rule 13.1 PCT.

Consequently, these claims are not unitary according to Rule 13 PCT.

C) Thus, the application is split into 2 groups of (alleged) inventions:

**Group I: Claims 1-40**

A method and a device including a microfluidic network for establishing flow of a first liquid in a channel,  
contacting at least a portion of the liquid with a reaction area;  
absorbing at least a portion of the liquid with an absorbent material contained in a liquid containment region positioned downstream of the reaction area, and  
controlling a rate of flow of a liquid in the channel, wherein the act of absorbing does not substantially modulate the flow rate of a liquid flowing in the channel upstream of the liquid containment region, solving the problem to handle liquids for an analysis.

**Group II: Claim 41**

A device including a microfluidic network, comprising:  
a first channel;  
a reaction area in fluid communication with the first channel; and  
an absorbent material and a disinfectant stored in a liquid containment region prior to use of the device, the liquid containment region positioned downstream of the reaction area and in fluid communication with the reaction area during use of the device, solving the problem to neutralize a reactant within the device.

According to Article 17(3)(a) PCT the ISA shall establish the International Search Report on those parts of the International Application which relate to the invention first mentioned in the claims, i.e. the above mentioned **group I**.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

2. Reference is made to the following documents:

- D1: EP-A-0 430 248 (MOCHIDA PHARM CO LTD [JP]) 5 June 1991 (1991-06-05)  
D2: EP-A-0 281 201 (PB DIAGNOSTIC SYSTEMS INC [US]) 7 September 1988 (1988-09-07)  
D3: WO 2005/072858 A (HARVARD COLLEGE [US]; SIA SAMUEL K [US]; LINDER VINCENT [CH]; WHITESID) 11 August 2005 (2005-08-11)

3. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of **claims 19 and 20** is not new in the sense of Article 33(2) PCT.
- 3.1 Document D1 discloses (the references in parentheses applying to this document) a microfluidic device (Fig.5) comprising an inlet (10), a reservoir (70), a channel (51), and at least one reagent-immobilized area (30) in the downstream of the inlet. The channel has a vent mechanism (20) and also a fluid sump (90) downstream of the reagent-immobilized area including an absorbent material (81) located in a absorbent material-accommodating area (80). A fluidic sample and a wash solution are introduced sequentially in the microfluidic device thorough the inlet and flows in the channel to the reagent-immobilized area where a chemical reaction takes place. All the liquids are finally absorbed in the absorbent material and retained therein (p.13, lines 28-43). Thereby the subject-matter of **claims 19 and 20** is known (Article 33(2) PCT).
- 3.2 Document D2 discloses (the references in parentheses applying to this document) a microfluidic device (Fig.1 and Fig.2) comprising two reservoir ((24) and (28)) having a reagent and a washing solution, in fluid communication with a first channel (passway (40)), a capillary tube (149 including at least one surface which has bonded to at least a portion thereof a first reagent which is capable of interacting with the analyte of interest present in a sample, a waste reservoir (46) including a liquid absorbent (48) and open areas ((50) and (52)) to retain all the waste sample, reagent, and other liquids, and an air hole in the top surface (55) to allow the waste liquids to fill the reservoir. Further the device is provided with means for passing the reagent or wash solution under pressure into the capillary (therefore controlling the flow rate). Thus the subject-matter of **claims 19 and 20** is known (Article 33(2) PCT).

4. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of **claim 1** does not involve an inventive step in the sense of Article 33(3) PCT.
- 4.1 The closest prior art is document D1 and discloses a microfluidic device and a method for using it, as assessed above in point 3.1. The subject-matter of claim 1 differs therefrom in that a flow of a first plug comprising a first liquid and a second plug comprising a second liquid in a channel of the device is established, wherein the first and second plugs are separated by a fluid immiscible with the first and second liquids.  
The technical effect of this difference is that it becomes possible to control the flow of different fluids in a channel without mixing them. Therefore, the problem to be solved by the present invention is how to modify the method in order to manipulate different fluids in a channel without mixing them.  
In this respect, document D3 discloses a method and device (Fig.13-Fig.15) for storing and/or delivering fluids, wherein at least a first and a second fluid, such as chemical or biochemical reagents or rinse solutions, are maintained separately from each other in a common vessel and transferred in series from the vessel to a reaction site to carry out a predetermined chemical or biochemical reaction. The transfer is made using a cartridge, which is later connected to a microchannel having a reaction area. Further the separation may be achieved interposing a third fluid (gas or hydrophobic fluids immiscible with aqueous fluids, p.18, lines 25-33)). The person skill in the art would acknowledge that using the cartridge shown in the device of D3, containing the different fluids separated by an immiscible fluid, in the microfluidic device in D1 would solve this problem without the need for inventive skill to the subject-matter of claim 1. The subject-matter of **claim 1** is thereby not inventive (Article 33(3) PCT).
5. The features of dependent **claims 2-18, 21-40** are either already known from D1, D2, and D3 (see passages cited in the Search Report) or represent well known alternatives to the skilled person and therefore cannot give rise to novelty and/or inventive step (Article 33(2)(3) PCT).

#### Re Item VIII

#### **Certain observations on the international application**

6. Although **claims 1 and 19** have been drafted as separate independent claims, they appear to relate effectively to the same method and to differ from each other only with regard to the definition of the method for which protection is sought and in respect of the terminology used for the features of that method. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.
7. Claims 10 and 16 relate to a method using a third liquid which is only defined in claim 9. **Claims 10 and 16** are thus unclear (Article 6 PCT).
8. The term "reservoir associated with the device" in claim 20 is not clear, because the device comprises the reservoir, therefore is not clear what is meant with "associated". Thus **claim 20** is not clear (Article 6 PCT).
9. According to the requirements of Rule 10.2 PCT, the terminology and the signs shall be consistent throughout the application. This requirement is not met in view of the use of the expressions "first channel", "microfluidic channel" and "first microfluidic channel" for the same feature (see **claims 20, 25, 31 and 33**).
10. The term "absorbent material is not accessible via the outlet" in claim 24 is not clear, because the absorbent material is in fluid communication with the outlet, therefore is not clear the meaning of "not accessible". Thus **claim 24** is not clear (Article 6 PCT).
11. The term "reaction area is not associated with an absorbent material" in claim 37 is not clear, because it is not clear which features define this association. Thus **claim 37** is not clear (Article 6 PCT).
12. Amended claims should be drafted in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).
13. The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2008/010022

14. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 is not mentioned in the description, nor are these documents identified therein.

## Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)

### General information

For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.

### Amending claims under Art. 19 PCT

Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.

### Filing a demand for international preliminary examination

In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/ WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT).

If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).

### Filing informal comments

After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.

### End of the international phase

At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).

### Relevant PCT Rules and more information

Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003